UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,706	08/24/2000	Keith V. Wood	341.005US1	3329

21186 7590 09/03/2009

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
09/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com
request@slwip.com

Office Action Summary	Application No.	Applicant(s)	
	09/645,706	WOOD ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,24,35-39,41-45,47,56,81,82 and 87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 24, 35-39, 41-45, 47, 81, 82, 56, 87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/09, 7/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/31/09 has been entered.

Claims 2-23, 25-34, 40, 46, 48-80, 83-85, and 88-96 have been canceled. Claims 1, 24, 35-39, 41-45, 47, 81, 82, 86, and 87 are at issue and are present for examination.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 24, 35-39, 41-45, 47, 81, 82, 86, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherf et al. (US Patent 5,670,356) in view of Zolotukhin et al. (US Patent 5,874,304), Donnelly et al. (WO 97/47358), Pan et al., Cornelissen et al. (US Patent 5,952,547), Hey et al. (US Patent 6,169,232) and Wood et al. (WO 99/14336).

Sherf et al. teach a modified firefly luciferase gene in which 14% of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells and eliminate restriction sites and sequences which encode transcription factor binding sites for known mammalian transcription factors including ATF, AP1, Sp1, AP2 etc. which would interfere with its genetically neutral behavior expected of a reporter gene. The altered gene includes at least 6 fewer transcription factor binding sites and was inserted into several mammalian expression vectors. The altered gene is transcribed and translated efficiently in mammalian host cells. The altered luciferase differs from the variant nucleic acids of the claims in that 25% or more of the codons were not altered. Sherf et al. further disclose that similar modifications could be made to other luciferase genes including click beetle luciferase genes.

Zolotukhin et al. teach a modified *Aequorea victoria* GFP gene in which 37% of the codons have been altered (and optionally up to even 80-90% may be altered) without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells. The optimized gene is inserted into an expression vector including a Kozak consensus sequence preceding the ATG initiation codon which optionally may include a multiple cloning site positioned between the promoter and the humanized GFP gene and/or downstream of the GFP gene. The altered gene preferably includes CTG codons encoding leucine, GTG or GTC codons encoding valine, GGC codons encoding glycine, ATC codons encoding isoleucine, CCT codons encoding proline, CGC codons encoding arginine, AGC codons encoding serine, ACC codons encoding threonine, and GGC or GGT codons encoding alanine and is transcribed and translated 5-10 times more efficiently in human cells than the wild type gene.

Donnelly et al. teach a modified hepatitis C virus core antigen gene in which 61% of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells and eliminate sequences which encode undesired sequences (such as ATTTA sequences, intron splice

sites, etc.) generated by the alteration of the natural codons (see pages 17-18).

Pan et al. teach a modified *Plasmodium falciparum* gene in which a large number of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for human host cells and eliminate sequences which might be detrimental to transcription and translation of the synthetic gene including sequences of promoters, poly A signals, intron splice sites and long runs of purines which might act as transcriptional termination sequences (see pages 1095). It should be noted that the elimination of undesired sequences was performed after the modification of the codon preference and thus would eliminate undesired sequences artificially introduced by the change in codons. The modified gene was successfully expressed in a variety of host cells (see page 1096) while expression of the unmodified gene has turned out to be difficult if not impossible (see page 1095).

Cornelissen et al. teach a modified *Bacillus thuringiensis* gene in which a small number of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to eliminate sequences which might be detrimental to transcription and translation of the

synthetic gene and particularly to eliminate sequences of cryptic promoters or DNA regulatory elements thereof which specifically interact with nuclear proteins (i.e., transcription factor binding sequences), see column 5, line 55 - column 6, line 15), and intron splice sites. The modified gene was successfully expressed in transgenic plants.

Hey et al. teach a plant sink protein gene in which a large number of the codons have been altered without altering the protein coding sequence such that the altered sequences were designed to optimize the codon selection for plant host cells and eliminate sequences which might be detrimental to transcription and translation of the synthetic gene including sequences of promoters, or elements thereof such as TATA box regions (i.e., a transcription factor binding sequence), poly A signals, intron splice sites, transcriptional termination sequences and runs of 4 or more pyrimidines which might interfere with transcription (see columns 9-12). It should be noted that the elimination of undesired sequences was performed after the modification of the codon preference and thus would eliminate undesired sequences artificially introduced by the change in codons.

Wood et al. teach a gene encoding a yellow green click beetle luciferase gene (wild-type Luc*Ppl*YG) having 100% identity

to SEQ ID NO:23 and 97% identity to the protein encoded by SEQ ID NO:2 herein.

Therefore, it would have been obvious to one of skill in the art to optimize the expression of the yellow-green click beetle luciferase gene of Wood et al. in human cells as taught by the combined disclosures of Sherf et al., Zolotukhin et al., Donnelly et al., Pan et al., Cornelissen et al., and Hey et al. to both increase the codon preference for humans as each of Zolotukhin et al., Donnelly et al., Pan et al. and Hey et al. each teach modifying a large percentage of the codons of a gene to be expressed in a host of interest and to remove potential promoter sequences, transcription binding factor sites, polyadenylation sites and splice sites as each of Sherf et al., Donnelly et al., Pan et al., Cornelissen et al. and Hey et al. each teach modifying at least several codons of a gene to be expressed in a desired host cell to match the codon preference of the host cell and/or to eliminate undesired sequences in order to increase its expression in the desired host cell and therefore increase its usefulness as a reporter gene in human and other desired host cells. One would have had a reasonable expectation of success in view of the results of the cited references which show that such alterations of other genes

substantially improve the levels of expression in a desired host.

Applicants argue that none of the cited documents discloses or suggests any of SEQ ID NO:9, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 297, SEQ ID NO: 299, or SEQ ID NO: 301, and thus that none of the cited documents discloses or suggests sequences that are structurally related to any of SEQ ID NO:9, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 297, SEQ ID NO: 299, or SEQ ID NO: 301, e.g., sequences that have at least 95% nucleic acid sequence identity to those sequences or that hybridize to those sequences or sequences complementary thereto under high stringency conditions, as recited in claims 1 and 47. However, while the examiner agrees that none of the cited documents discloses or suggests any of SEQ ID NO:9, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 297, SEQ ID NO: 299, or SEQ ID NO: 301 and claims limited to specifically these nucleic acids would be allowable, the cited references do suggest nucleic acids structurally related thereto as is claimed. The rejection specifically suggests altering a parent nucleic acid which encodes a protein similar or identical to SEQ ID NO:23 (such as the nucleic acid of Wood et al.) by codon optimization and removal of unwanted sequences created by the optimization as taught by the cited references. Following the suggestions of

Zolotukhin et al. with regard to specific codon optimization choices for high level expression in human cells followed by modifications to eliminate undesirable sequences as taught by the secondary references, while not leading a skilled artisan to the specific nucleotide sequence of SEQ ID NO:9, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:18, SEQ ID NO:297, or SEQ ID NO:301 (as this would require that the art suggest all of applicants specific modification choices) would lead a skilled artisan to produce a optimized sequence which would hybridize to SEQ ID NO:7, SEQ ID NO:9 and SEQ ID NO:297 under high stringency conditions as high stringency hybridization conditions still allow for a substantial number of positions (i.e., up to approximately 5% of the total; i.e., approximately 81 nucleotides in this case) in which the individual choices could be different. It is noted that this rejection as presented here was upheld by the Board in the decision mailed 9/3/08.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re*

Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 24, 35-39, 41-45, 47, 81, 82, 86, and 87 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8, 9, 11-13, 15, 18-21, 24-45, 47, and 60-62 of copending Application No. 11/786,785. The rejection is explained in the previous Office Action.

Applicants note that the instant rejection is merely provisional and thus state that a terminal disclaimer is not required at this time. While examiner acknowledges that the instant rejection is a provisional rejection and that as such a terminal disclaimer may not be needed for the allowance of the instant claims, the rejection will be maintained as long as there is patentably indistinct claims present in both applications.

The provisional ODP rejection over 11/825,304 is withdrawn in view of the amendments to the instant claims to limit the scope of claimed nucleic acids to optimized variants of nucleic acids encoding click beetle luciferases while the claims of the copending application recite optimized variants of nucleic acids encoding firefly luciferase.

The references lined through on applicants IDS were not considered as they are not in the English language and no statement of their relevance was submitted.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action

is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652